

## Case report

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# Penile calciphylaxis in a patient with end-stage renal disease: a case report and review of the literature

<https://doi.org/10.1515/med-2018-0025>

received January 26, 2018; accepted March 19, 2018

**Abstract:** Penile calciphylaxis is a rare cause of penile gangrene that presents in patients with end-stage renal disease. The rates of comorbidity and mortality of penile calciphylaxis are extremely high. Unlike other penile gangrene, such as Fournier's gangrene, the benefit of aggressive surgical therapy is controversial. Here we present a case of penile calciphylaxis in a 43-year-old man with end-stage renal disease on hemodialysis. He received total penectomy but died due to multisystem complications 2 weeks after surgery. We review the literature on the management options and outcomes in patients with penile calciphylaxis.

**Keywords:** Penile calciphylaxis; Penile gangrene; Penectomy; End-stage renal disease; Microcalcification

## 1 Introduction

Calciphylaxis is a serious systemic disorder of smaller arteries, arterioles and capillaries seen in 1% to 4% of patients with end-stage renal disease on hemodialysis and is usually associated with elevated calcium-phosphate product [1]. It is a clinical condition with mortality rate higher than 60% [2]. Penile calciphylaxis is rare because of its rich vascular network and the prognosis is also poor, with a reported overall mortality rate of 64% and mean time to death of 2.5 months [1,3]. The benefit of penectomy is still under debate. Herein, we present a hemodialysis-dependent diabetic patient who presented with subacute distal penile dry gangrene due to penile calciphylaxis, and review the pertinent medical literature.

## 2 Case report

A 43-year-old man presented with fever, chills and a purulent sternotomy wound. He had a history of end-stage renal disease for which he had been treated with hemodialysis for 6 years, poorly controlled type II diabetes mellitus, hypertension, and double vessel coronary artery disease. He had undergone coronary artery bypass graft surgery 2 months before this presentation, and received debridement for a sternotomy wound infection and pectoralis major myocutaneous flap rotation 1 month before this presentation. One month after admission, he presented with dry gangrene of the distal third of the penis, including the glans and part of the shaft for 7 days (Figure 1). Dry gangrene was also present in both feet, the right ankle and thigh. Serum phosphate was 6.7 mg/dL (2.7-4.5 mg/dL), calcium was 9.8 mg/dL (8.9-10.3 mg/dL), calcium-phosphate product was 65.7 mg<sup>2</sup>/dl<sup>2</sup> (20.6-52.5 mg<sup>2</sup>/dl<sup>2</sup>), albumin was 2.4g/dL (3.5-5.0 g/dL), HbA1c was 9.0%, and BMI was 24.8kg/m<sup>2</sup>. He did not take any anticoagulant medication, such as Warfarin. Computed tomography of his abdomen showed severe diffuse vascular cal-

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cifications, including in the branches of bilateral internal iliac arteries (Figure 2). Due to penile pain and progression of necrosis of the distal penis, penectomy was performed. The intraoperative findings after penile degloving showed extensive ischemic damage, and the spongiosal and cavernosal tissues of the pendulous part of the penis showed no signs of vitality. After incision of the cavernous bodies, only blood clots were drained, and therefore we performed total penectomy and perineal urethrostomy. Plastic surgeon consultation suggested not to resect other extragenital gangrene due to patient's poor condition. The pathological report showed microcalcifications in the stroma and vascular wall consistent with calciphylaxis (Figure 3). Dyspnea and conscious disturbances occurred after three days antibiotics usage for post-operative fever. His overall condition deteriorated and died of respiratory failure and sepsis 2 weeks later.

**Ethical approval:** Research has been complied with all the relevant national regulations, institutional policies and in accordance the tenets of the Helsinki Declaration.

**Informed consent:** Informed consent has been obtained from all individuals included in this study.

### 3 Discussion

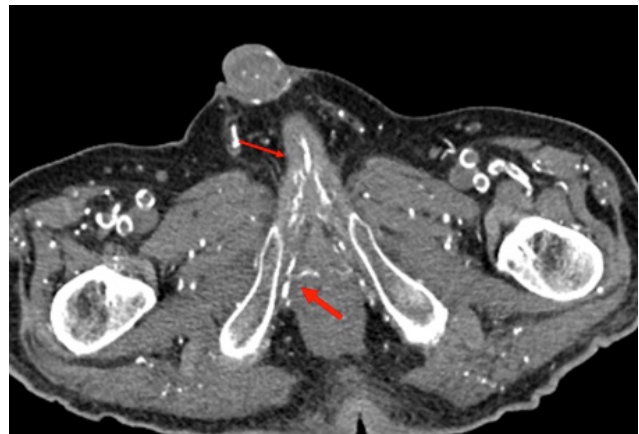
Calciphylaxis is characterized by medial calcification and intimal fibrosis of medium and small arteries. Mottling of the skin and induration in a livedo reticularis pattern



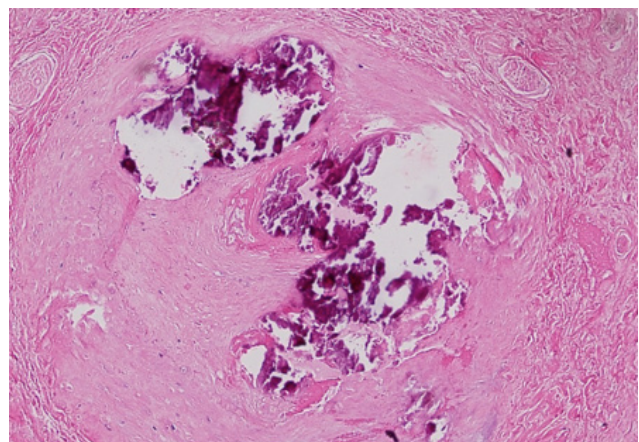
**Figure 1:** Gangrenous penis.

is a characteristic clinical presentation of calciphylaxis, which generally affects the distal extremities, buttocks, and thighs, and sometimes the penis. Penile calciphylaxis has an extremely poor prognosis, with a reported overall mortality rate of 64% and mean time to death of 2.5 months [3]. Cimmino et al. recommend penile biopsy unnecessary for diagnosis of penile calciphylaxis [4].

A total of 50 cases of penile calciphylaxis have been reported in the English literature (Table 1) [2-41]. The average age was 54.5 years (range 32 to 81). Including our case, all patients had end stage renal disease, 42 patients received hemodialysis, 7 patients received peritoneal dialysis and 2 patients were in the pre-dialysis stage. Forty-one patients had diabetes mellitus. Average calcium level was 9.2 mg/dl, average phosphate level was 8.0 mg/dl and average calcium-phosphate product was 72.8 mg<sup>2</sup>/dl<sup>2</sup>. The overall mortality rate was 56.5%. Three-month mortality rate was 47.8%. Mean time to death was 97 days and median time to death was a month. There was no



**Figure 2:** Internal pudendal (large arrow) and penile artery (small arrow) calcification seen on computed tomography.



**Figure 3:** Calcifications in the vascular wall within the gangrenous penile shaft.

**Table 1:** Review of reported cases of penile calciphylaxis with end-stage renal disease.

Authors	Age	Ca (mg/dl)	P (mg/dl)	CaP (mg <sup>2</sup> /dl <sup>2</sup> )	PTH (pg/mL)	extragenital gangrene	penectomy	parathyroidec- tomy	3-month prognosis
MMH	43	9.8	6.7	65.7	no data	yes	yes	no	death
Ivker RA[5]	43	9.2	5.6	51.5	375	yes	no	yes	alive
Ivker RA[5]	58	7.9	6.4	50.6	89	yes	yes	yes	alive
Melikoglu M[6]	48	7.4	11	81.4	no data	yes	yes	no	death
Wood JC[7]	56	8.9	9	80.1	1280	yes	yes	yes	alive
Jhaveri FM[8]	62	9.3	9.5	88.4	74	yes	no	no	death
Jhaveri FM[8]	44	10.5	7.6	79.8	1450	yes	no	yes	alive
Jhaveri FM[8]	44	10	10.2	102	405	yes	no	yes	loss
Jhaveri FM[8]	41	10.6	7.1	75.3	746	yes	no	no	death
Jhaveri FM[8]	59	10.3	7.4	76.2	89	yes	no	yes	death
Siami GA[9]	44	7.9	8.6	67.9	no data	yes	yes	no	death
Boccaletti VP[10]	72	10.5	7.8	91.9	881	no	no	no	death
Rich A[11]	34	no data	no data	no data	no data	yes	yes	no	death
Jacobsohn HA[12]	60	9.7	9	87	430	yes	yes	no	death
Karpman E[3]	59	7.9	9.6	75.8	379	yes	yes	no	death
Barthelmes L[13]	48	no data	no data	no data	no data	no	yes	no	death
Oikawa S[14]	32	no data	no data	no data	63	yes	no	yes*	death
Rifkin BS[15]	61	no data	no data	no data	no data	yes	no data	no data	loss
Woods M[16]	35	8.4	7.4	62.2	38	no	yes	no	death
Halachmi S[17]	57	8.5	8.5	76.5	375	yes	no	no	death
Agarwal MM[18]	52	8.5	7.5	63.8	no data	yes	no	no	death
Sorensen MD[19]	65	8.5	no data	no data	121	no	yes	no	alive
Ohta A[20]	41	9.8	5.2	51	18	yes	yes	no	alive
Rizvi T[21]	72	7.4	7.3	54	315	no	no	no	alive
Bhatty TA[22]	39	no data	7.1	no data	344.7	yes	no	no	alive
Sandhu G[23]	58	10.2	10.3	105.1	82	no	no	no	alive
Bappa A[24]	72	9.6	7.3	70.1	315.2	yes	no	no	loss
Shah MA[25]	72	7.9	6.6	52.1	164	yes	no	no	death
Prematilleke I[26]	66	10.4	5.9	61.4	30.8	no	yes	no	death
Prematilleke I[26]	38	9.9	7.7	76.2	48	no	yes	no	alive
O'Neil B[27]	72	8.9	5	44.5	1462	no	yes	yes	alive
O'Neil B[27]	59	no data	no data	no data	816	yes	yes	yes	alive
O'Neil B[27]	64	8	8.1	64.8	516	no	yes	yes	alive
Akai A[28]	36	no data	no data	56	no data	yes	no	no	alive
Kumar V[29]	73	8.8	11.8	103.8	633	no	no	no	alive

**Table 1 continued:** Review of reported cases of penile calciphylaxis with end-stage renal disease.

Barbera V[30]	50	12.8	8.6	110.1	615	no	yes	no	alive
Yecies T[31]	33	no data	no data	no data	no data	no	yes	no	alive
Cimmino CB[4]	62	9	8.4	75.6	no data	no	no	no	alive
Cimmino CB[4]	38	8.7	no data	no data	no data	yes	no	no	loss
Cimmino CB[4]	49	7.4	9.6	71	799.8	no	no	no	loss
Haider I[32]	61	no data	no data	no data	260	yes	no	no	death
Morrison M[33]	60	no data	no data	no data	no data	yes	no	no	alive
Hanna RM[34]	64	9	13.5	121.5	612	yes	yes	no	alive
Sarkis E[2]	54	no data	no data	no data	94	yes	no	no	death
Malthouse T[35]	61	9.1	8.4	75.9	155	yes	no	no	death
Shiraki T[36]	76	no data	no data	42	127	yes	no	no	alive
Endly D[37]	58	9	4.1	39.8	410	yes	no	no	death
Bashir SO[38]	46	9.5	7.4	70.3	600	no	no	yes	alive
Maselli G[39]	64	no data	no data	no data	no data	no	no	no	alive
Campbell RA[40]	46	10.7	6	64.2	1096	no	yes	no	alive
Olaoye OA[41]	81	9.8	8.4	82.3	1131	no	no	no	death

Ca, calcium; P, phosphate; CaP, calcium-phosphate product; PTH, parathyroid hormone

\* Calciphylaxis was developed after parathyroidectomy.

correlation between mortality rate and age, diabetes mellitus, calcium level, phosphate level and calcium-phosphate product level.

Parathyroid hormone level was reported in 38 patients and average parathyroid hormone level was 458.9 pg/ml. Secondary hyperparathyroidism was found in 33 patients. One patient underwent parathyroidectomy before and 10 patients underwent parathyroidectomy after calciphylaxis developed. The 3-month mortality rates were 33.3% and 60% in patients undergoing parathyroidectomy after calciphylaxis and patients without parathyroidectomy, respectively ( $P=0.18$ ). Mortality rate was not correlated with parathyroid hormone level and parathyroidectomy. This finding was different from that reported by Karpman et al., who suggested that parathyroidectomy may improve survival [3]. The possible reason for the difference was that they included patients without documented parathyroid hormone level in their statistics.

Extragenital gangrene was noted in 32 patients. The 3-month mortality rate was higher in patients with extragenital gangrene than in those without extragenital gangrene (60.7% vs. 27.8%,  $p=0.03$ ). Extragenital gangrene involves more blood vessels and may result in worse prognosis.

Twenty-one patients received partial or total penectomy. The mortality rates were 42.9% and 52% in patients undergoing partial or total penectomy and patients who received local debridement and wound care, respectively ( $P=0.54$ ). Karpman et al. also reported no statistically significant difference in survival between patients treated with penectomy and those treated with local debridement and wound care [3]. Since penectomy showed no survival benefit, we suggest that penectomy should be considered in the presence of severe pain refractory to analgesics or uncontrolled infection.

Akai A et al. reported a case of penile calciphylaxis who underwent femoral artery to deep dorsal penile vein bypass [28]. After revascularization surgery, pain subsided and the wound healed. Shiraki T et al. reported a case of penile calciphylaxis successfully treated with internal iliac artery balloon-expandable bare metal stent implantation [28]. Two cases were treated with hyperbaric oxygen therapy but both of them died within a month [12,14].

Three cases were treated with sodium thiosulfate, and 2 patients survived [2,23,33]. The possible mechanism of sodium thiosulfate is chelation of calcium ions, dissolution of insoluble calcium deposits and restoration of endothelium [2]. In a retrospective study of 27 patients

with calciphylaxis in other locations, 52% resolved with sodium thiosulfate administration [2].

Penile calciphylaxis is a rare disease with poor prognosis because calciphylaxis involves smaller arteries, arterioles and capillaries systemically. Unlike other penile gangrene, such as Fournier's gangrene, the benefit of aggressive surgical therapy is controversial. Patients with extragenital gangrene have higher rates of mortality. Due to its rarity, there is no consensus regarding the treatment of this disease. Conservative treatment, sodium thiosulfate, hyperbaric oxygen, internal iliac artery stent, revascularization surgery, penectomy and parathyroidectomy have all been described. Literature review showed that penectomy and parathyroidectomy had no significant survival benefit. However, since there is no definite curative treatment, physicians may attempt combining different treatment modalities.

**Conflict of interest statement:** Authors state no conflict of interest.

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